

Gynecomastia

Def Increase the size of glandular tissue of the male breast and felt as firm mass inside breast soft tissue.

- D.D
- ① Lipomastia increase mass content of the breast in obese
 - ② Breast Cancer, unilateral, Rare, Mammography is indicated
 - ③ Prolactin secreting adenoma of pituitary gland.
 - ④ Oestrogen " tumour in adrenal medulla or testis.

Causes Any condition lead to Oestrogen/Androgen Imbalance
↑ Oestrogen production or ↓ Androgen production.

Oestrogen secreted directly from Leydig cell (15%) and (85%)

Converted from Androgen in Liver, Adipose tissue.

① Physiological Gynecomastia:

- ① Neonatal → placental transfer of oestrogen
- ② Pubertal → ↑ production of oestrogen before production of Androgen
- ③ Advanced age → ↓ androgen + ↑ oestrogen conversion

② Pathological Gynecomastia:

- ① 1ry, 2ry testicular disorders that lead to ↓ androgen, ↑ prolactin.
- ② Drugs, systemic disorders

- ③ Neoplastic → endocrine active tumours (testicular tumours) (Adrenal cortex tumour) (Ectopic HCG) secretion by tumours of Lung, Liver, Kidney

Diagnosis :- ① Examination. ② Investigation of Systemic Disease. ③ Investigation of endocrine disease

③ Hormonal profile (LH, FSH, testo, Prolactin) Liver F, Kidney

④ u/s, CT, MRI

Treatment Medical / Tamoxifen / danazole / testosterone
plastic surgery if it's large size more than 3 cm

Hyperprolactinemia

Normal serum prolactin level 15-20 ng/mL

Controlled by balance between

1. Inhibition (Dopamine) secreted from Hypothalamus and transported to pituitary gland by pituitary stalk.
2. Stimulation By PRF prolactin Releasing Factor.

Prolactin may increase physiologically \rightarrow during sleep, stress, exercise

Causes of Hyperprolactinemia:-

- ① Prolactinoma prolactin secreting tumours. micro prolactinoma less than 1cm / Macro prolactinoma more than 1cm proliferate and destruction of surrounding structure (optic nerve) S. prolactin > 100 ng/mL prolactinoma + pancreatic + parathyroid (MEN) Multiple endocrine neoplasia
- ② Craniopharyngioma tumor in ~~stalk~~ between 2 lobes of Pituitary lead to compression on stalk \rightarrow interruption of inhibition of Dopamine ~~TRF~~ Secreted by hypothalamus $\rightarrow \uparrow$ prolactin.
- ③ Thyroid disorders Hypothyroidism $\rightarrow \uparrow$ Thyrotropin TRF Releasing Factor from hypothalamus which is stimulant of prolactin secretion.
- ④ Hepatic / Renal $\rightarrow \downarrow$ metabolic clearance of prolactin.
- ⑤ Drugs \rightarrow TCA, Phenothiazine, α methyl dopa, Oestrogens
- effects
Hyperprolactinemia \rightarrow inhibition of pulsatile GnRH release $\rightarrow \downarrow$ FSH, LH, testosterone and defective spermatogenesis.

Prolactinomas \rightarrow direct effect on pituitary cells $\rightarrow \downarrow$ FSH, LH

Diagnosis CP headache, visual field, Cynemastia, discharge, \downarrow ED, retrograde ejaculation

Hormonal $\rightarrow \uparrow$ prolactin + \downarrow FSH, LH, testosterone

\downarrow semen parameters / MRI, CT in microprolactinoma

3 Bromocriptine (Parlodel) ^{Treatment}

2 Dopamine agonist

2 S.E

① Hypotension

② Nausea

Constipation

So the dose is gradually increase
Dizziness, nasal stuffiness

Cabergoline (Dostinex)

Dopamine agonist.

Tolerated

selective, Potent, well ~~to~~

Duration of action may reach 3 weeks

= Sildenafil citrate =

Selective ~~PDE~~ PDE inhibitor

PDE enzyme has 6 isotopes the most important one is isotope type (5) responsible for $\downarrow cGMP \rightarrow \uparrow Ca^{+} \rightarrow$

Contraction of C. cavernosa.

Sildenafil is a selective PDE inhibitor type (5)

Dose 50 — 200mg. the usual dose is 50 taken (0.5h — 4h) before Coitus

Therapeutic effect

- it's enhancer of agent rather than erection inducer
- better if taken on empty stomach.
- it's good in Psychogenic, ED less effect on organic ED

S.E Headache, Facial flushing, indigestion, Myalgia
Visual disturbance. This is due to the presence of PGE₅ in other body tissues.

Drug interaction.

- Sildenafil depends on Cytochrome P₄₅₀ in metabolism so it interacts with drugs inhibit CYP₄₅₀ as Ketconazole, Erythromycin, itraconazole, cimetidine.
 - the action of sildenafil depends on NO/cGMP pathway it's contraindicated with pt on nitrates
- Non selective PDE inhibitors "pentoxifylline" pentoxifylline
Trental 400 1x3 x 12 weeks improve erection

U/S in male infertility

Diagnostic :-

- ⇒ Varicocele → Doppler Colour Doppler U/S ~~could~~
Spermatic venography
- ⇒ Epididymal obstruction →
Scrotal and transrectal U/S (TRUS)
and Congenital unilateral absence.
- ⇒ Ejaculatory duct obstruction in Azoospermia pti
or severe oligospermia (partial obstruction)
- ⇒ Median cyst → 2 types semen containing, Non semen containing.
it's obstructive if it compress the ejaculatory duct.
TRUS + MRI confirm the diagnosis
- ⇒ Seminal vesicle causes of ejaculatory duct obstruction.
Endoscope R ByTURED
- ⇒ Cryptorchism.
~~which~~ undescended test, localization (ingul, Abd)
- ⇒ Scrotal mass
 - ⇒ extratesticular → (inguinal hernia, epididymal mass, varicocele)
 - ⇒ intratesticular → (Seminoma, teratoma, Lymphoma, Sertoli cell
Leydig cell tumours)
- ⇒ Testicular microlithiasis (TM)
Calcification within the testis.
- ⇒ Pituitary adenoma → prolactin-producing adenomas
Confirmed by MRI, ~~do~~
- ⇒ Renal disorders → unilateral renal agenesis
in cases of Congenital Bilateral Absence of vas (CBAVD) or unilateral
+ polycystic kidney

Image-guided treatment :-

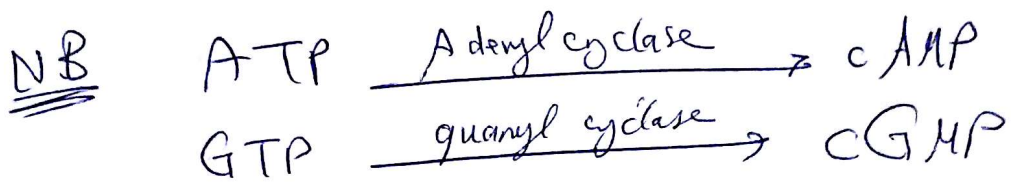
- ① obstructive azoospermia TRUS
- ② Median cyst puncture and seminal vesicle Aspiration guided BY TRUS. in cases of ejaculatory duct obstruct
- ③ Seminal vesiculography + ~~FBI~~ TURED
- ④ Ejaculatory duct dilatation (ballooning)
- ⑤ Percutaneous engraftment of varicocele
- ⑥ image guided in TESE
- ⑦ doppler US can detect the suitable sites of spermatogenesis help in micro TESE
- ⑧

Phosphodiesterase inhibitors

Penile erection depends on Relaxation of the smooth muscles. Relaxation ~~is~~ done by \downarrow intracellular Ca^{2+} . By \uparrow cAMP, cGMP cause they promote Ca^{2+} to bind to Ca^{2+} binding protein.

So the aim of erection is to \uparrow cAMP, cGMP phosphodiesterase enzyme deactivate the formation of cAMP, cGMP.

So phosphodiesterase inhibitors $\rightarrow \uparrow$ cAMP + cGMP
 $\rightarrow \downarrow$ intracellular $\text{Ca}^{2+} \rightarrow$ ~~relaxation~~ \rightarrow erection.



ex Papaverine $\rightarrow \uparrow$ cAMP
Sildenafil $\rightarrow \uparrow$ cGMP

Nitric oxide (NO)

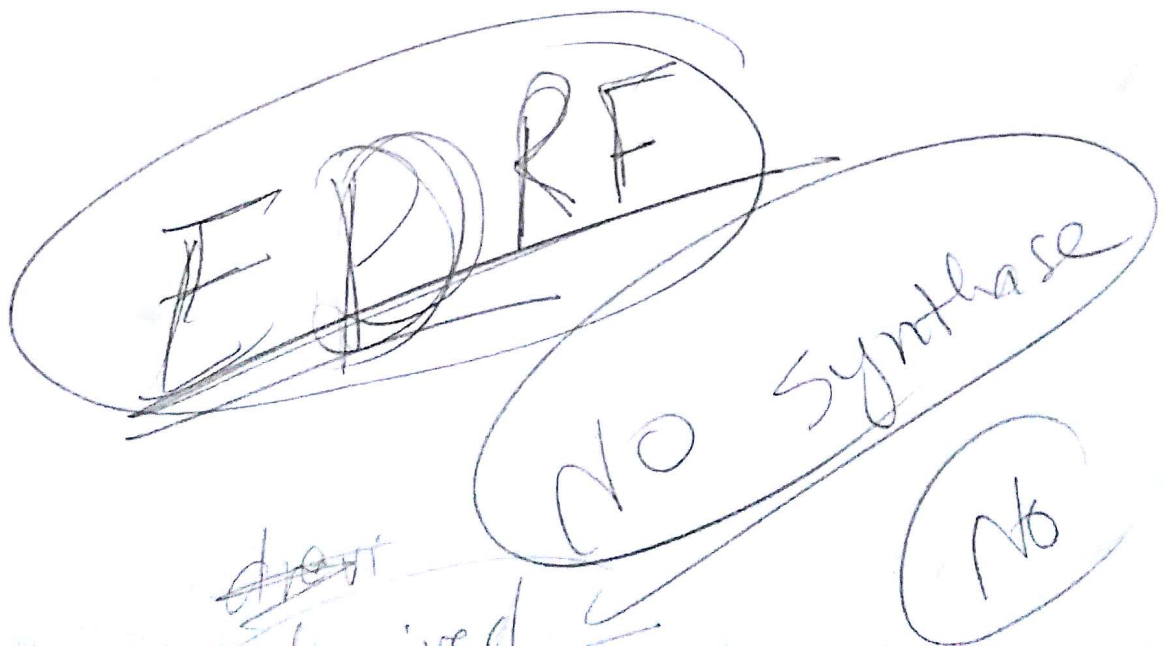
endothelium derived Relaxing Factor
it's synthesized from L-arginine (Amino acid) under the effect of NO synthase. in the vascular endothelium
~~it's synthesized~~ this process depends on the presence of high P_{O_2} 100 mg/Hg. so that it's not done in venous blood. it occurs normally in placid penis in which arterial blood.

Mechanism of action.

By ~~increasing~~ ^{production} CGMP → ↑ intracellular cat

→ Relaxation of smooth muscle → erection.

→ Nitroglycerin Topical lead to release of (NO)



Environmental Gonadotoxins

[1] Ionizing radiation

Anti spermatogenic effect - Dose dependent - Direct damage of Spermatogonia - mini-satellite mutations and chromosomal damage

[2] Anti Cancer therapies:

Cytotoxic ~~drugs~~ ^{drugs} → gene damage → mutation or malformation.

[3] Pesticides: DBCP for control pest in banana

testicular damage - oligo - Azospermia, ↑ FSH, LH (irreversible damage)

[4] Complex Organo-chloride compounds

Teratogenic ex: Xenoestrogen if exposed prenatal woman inhibit testicular development.

[5] Smoking

- Cigarettes have hazard compound eg: acrolein oxidative damage of testis
- ↓ sperm motility. - genetic damage. - DNA damage in sperm
- smoking mother → ↓ Testicular size, cryptorchism.

[6] Life style

Cell phones → Electromagnetic waves → ↓ Fertility; ↓ motility, ↓ morphology, ↓ viability.

[7] Testicular hyperthermia

Hyperthermia → impair spermatogenesis

laptop - jacuzzi → ↓ semen parameters.

[8] Alcohol and illicit drugs.

- ED + ↓ libido + Gynecomastia.
- Alcohol have estrogenic effect → aromatization of testosterone
- Alcohol → ↓ antioxidant in the body → ↑ oxidative stress → ↓ sperm motility
- Marijuana → ↓ sperm density, motility, morphology
- opiates → ED, ↓ libido, suppress secretion of GnRH → ↓ LH → ↓ testosterone

Hemospermia

Presence of blood in semen (ejaculate)

Causes idiopathic (age)

[1] Infection The most common cause. infection of inflammation of prostate, glands, urethra. Epididymis ---

std gonorrhea, Trichomonas, Chlamydia. others bilharziasis, T.B

[2] Trauma

- physical Trauma → excessive masturbation, excessive hard intercourse
- after medical procedures → prostatic biopsy, injections for hemorrhoids radiation therapy, vasectomy. / pelvic fracture.

[3] Tumours and polyps, cysts

prostatic tumours (BPH, Cancer)

[4] prostatic calculi

[5] others: ABP, Liver cirrhosis, HIV, Leukemia, purpura,
Drugs → Anticoagulants.

(C/P) @ Colour is vary from red to brown, black according to cause, duration

@ Pain less/painful @ no decrease in Libido

Examination of prostate, vas, epididymis.

In T.B prostate is indurated, nodular, Calcification may be found

Investigation

[1] Urine: to exclude Itacnuria, Bilharziasis, Pyuria

[2] Semen: To ensure about Hemospermia, infection pus cells

[3] Semen culture → for chronic infection

- X-ray / ul's / urethroscopy urethroscopy

- Blood examination (PSA), Liver function

- Transrectal ultrasonography TRUS → evaluation of size, prostate ejaculatory duct,

Treatment of the cause + Diethylstilbesterol
5mg [1X/1X/7]